
بسم الله الرحمن الرحيم

Epidemiology and Pathophysiology of Hypertensive Kidney Disease

By

Dr.

Mahmoud Awad

Lecturer of Internal Medicine

Faculty of Medicine, Mansoura University

- Hypertension is both a cause and a consequence of C.K.D.
- The true prevalence of CKD throughout diagnosed hypertensive cases has not been established.
- The National Health and Nutrition Examination survey during 1999-2006
  - Prevalence of CKD among normal BP: 13.4%.
  - Prehypertension: 17.3%.
  - Undiagnosed hypertension: 22.0%
  - Diagnosed hypertension: 27.5%

- Recently published prospective data have shown that even in the absence of diabetes and atherosclerosis, high-normal blood pressure is associated with an almost 3-fold greater risk of future development of CKD.

- CKD is prevalent in undiagnosed and pre-hypertension. So, earlier identification and treatment of both these conditions may prevent or delay morbidity and mortality from CKD.
- The prevalence of hypertension, CKD and ESRD related to hypertension continues to rise worldwide.

- **In the US between 2003-2009:**
  - **The prevalence of CKD is high among individuals with undiagnosed or pre-hypertension.**
  - **The prevalence of CKD increases across the diagnostic spectrum of hypertension regardless of how kidney disease is defined.**
  - **CKD awareness is low among individuals with undiagnosed or pre-hypertension.**
  - **High BP is one of the leading causes of ESRD every year, hypertension causes more than 25.000 new cases of kidney failure in the united states.**
  - **Persons with all categories of blood pressure warrant further studies of appropriate CKD education, screening and prevention programs, as they are likely at high risk.**

- The actual prevalence of CKD related to hypertension is difficult due to the following causes:
  - Absence of uniform criteria to establish a diagnosis of hypertensive nephropathy.
  - Most of studies related to hypertension exclude cases with CKD.
  - High % of cases of hypertension were not aware of their diagnosis.
  - Prevalence of CKD in hypertensive cases significantly varies according to (Age, sex, race, culture, socioeconomic state, presence or absence of other risk factors …etc).

Pathophysiology of Hypertensive Kidney Disease

- Hypertensive renal disease (or “hypertensive nephropathy” or “hypertensive neprhosclerosis”) is a medical condition referring to damage to the kidney due to chronic high BP. It should be distinguished from “renovascular hypertnesion” which is a form of secondary hypertension.

- **The diagnosis of hypertensive nephrosclerosis is dependent on the exclusion of other primary renal diseases:**
  - **A careful past history, family history, search for signs for target organ damage, such LVH, hypertensive retinal change, careful urine microscopy, 24-h urinary protein, renal ultrasound, tests for glomeralonephritic or vasculitic diseases, such on approach was enough for diagnosis at about 90% of cases according to African-American Study on Kidney Disease and Hypertension (AASK).**

- **According to AASK renal biopsy for diagnosis of hypertensive nephropathy is indicated in clinical practice only when:**
  - **Substantial doubt based on the clinical evidence.**
  - **Patients who do not have accelerated hypertension.**
  - **A long history of hypertension with serum creatinine less than 3mg/dl and 24-h urine protein excretion more than 1.5 gm/24h.**

How does high blood pressure hurt the kidneys??

- High BP makes the heart work harder and overtime, can damage blood vessels throughout the body, if blood vessels in the kidneys are damaged, they may stop removing wastes and extra fluids from the body.
- The extra fluid in the blood vessels may then raise BP even more → more vascular damage in the kidneys → it's a dangerous cycle (United States Renal Data System 2007 "USRDS").

Robert B et al. (2003) said:

- In the kidneys, as a result of benign arterial hypertension, hyaline (pink, amorphous, homogeneous material) accumulates in the wall of small arteries and arterioles, producing the thickening of their walls and the narrowing of the lumina — hyaline arteriolosclerosis.
- Consequent ischemia will produce tubular atrophy, interstitial fibrosis, glomerular alterations and periglomerular fibrosis.
- Functional nephrons have dilated tubules, often with hyaline casts resulting in proteinuria and hematuria.

- **Suneel U et al. (2011) proposed two initial injuries that lead to kidney injury.**

A. Changes in extrarenal and renal vasculature associated with systemic hypertension → breakdown of elastic fibres in arterial circulation → progressive intimal thickening → afferent arterioles lose their autogregulatory capacity owing to hyalinosis and dilatation → the glomeruli suffer from the diseased state of the vasculature and lose their ability to autoregulate and become unable to attenuate hyperfiltration mediated injury --. More ischemia hypoxia and more loss of renal autoregulation.

B. Without BP control more vascular damage, ischemia, hypoxia → impaired function of endogenous vasodilators, ↑ sympathetic activity and ↑ salt retention → loss of ability to achieve complete sodium balance by the decrease in GFR → the pressure naturesis curve shifts to the left and Na+ balance is only achieved at the expense of an ↑ in BP → more and more ischemia, hypoxia, loss of autoregulatory renal functions → ↑ renal damage → vicious cycle → ↑ BP → progressive renal injury.

Historically, hypertension induced renal damage has been separated into 2 distinct clinical and histological patterns (Anil K, et al., 2004).

Benign nephrosclerosis:

- Uncomplicated hypertension.
- Non specific vascular lesions of hyaline arteriosclerosis.
- No overt proteinuria.
- Mild focal ischemic glomerular obscelence and nephron loss occur over time, renal function is not seriously compromised except in susceptible individuals such as blacks.

Malignant neprhosclerosis:

- Malignant hypertension.
- Characteristic renal phenotype of acute disruptive vascular and glomerular injury with prominent fibrinoid necrosis and thrombosis.

The pathogenetic determinants of hypertensive renal damage can be broadly reported into:

A. **The systemic BP load → discussed before.**

B. **The degree to which such load is transmitted to the renal vascular bed and autoregulatory responses and how provide the primary protection against hypertensive renal damage till this threshold is exceeded → acute disruptive injury (Benign → malignant nephrosclerosis).**

C. Local BP independent determinants of tissue susceptibility:

1. Genetic or acquired differences in intrinsic structure or function of the glomeruli may result in differences in the severity of damage expressed at any degree of hypertension (barotrauma).
2. The glomerular hypertrophy may be an independent risk factor for GS.

3. ↑ in wall tension (laplace law: tension = pressure x radius) → hypertrophy of glomerular capillaries → protective local mechanism but its ability is limited to maintain physical integrity and mechanical support during hypertensive stress → tissue damage resulting in:

- Damage of autoregulatory mechanisms
- Damage promoting effects of angiotensin II and aldosterone.
- Oxidative stress.
- Activation of growth factors and fibrogenic mediators such as TGF-B and plasminogen activator inhibitor-1.

4. All these local intrinsic factors → ↑ susceptibility to tissue damage → benign and/or malignant GS.

Conclusion

- HTN is a worldwide problem.
- HTN is the 2nd leading cause of CKD worldwide.
- The actual prevalence is uncertain and requires more awareness and studies.
- The role of renal biopsy in diagnosis of hypertensive nephropathy is limited.
- The pathophysiology is variable, different, still unclear and requires more awareness and studies.


Thank You